

Applicants: Richard Deckelbaum et al.  
U.S. Serial No.: 10/033,629  
Filed: December 28, 2001  
Page 8

**REMARKS**

Claims 1-30 are currently pending, with claims 1-11, 15-17, and 24-25 under examination, and claims 12-14, 18-23, and 26-30 withdrawn from consideration. Applicants have hereinabove amended claims 1, 3, 10, 11, 15, 24, and 25, and canceled claims 4-9 without prejudice or disclaimer to applicants' right to pursue the subject matter of these claims in a future continuation or other application. Support for the amendments to claim 1 can be found in the specification as originally filed at, *inter alia*, page 14, line 26 to page 15, line 3. Support for the amendments to claim 3 can be found in the specification as originally filed at, *inter alia*, page 16, lines 5-8. Support for the amendments to claim 10 can be found in the specification as originally filed at, *inter alia*, page 20, lines 30-32. Support for the amendments to claim 11 can be found in the specification as originally filed at, *inter alia*, page 21, lines 8-10. Support for the amendments to claim 15 can be found in the specification as originally filed at, *inter alia*, page 22, lines 20-34. Support for the amendments to claim 24 can be found in the specification as originally filed at, *inter alia*, page 24, lines 19-29. Support for the amendments to claim 25 can be found in the specification as originally filed at, *inter alia*, page 25, lines 31-34. Applicants maintain that the amendments to the claims raise no issue of new matter. Accordingly, after entry of this Amendment, claims 1-3, 10-11, 15-17, and 24-25 will be pending and under examination.

**Claims Rejected Under 35 U.S.C. §112 (Second Paragraph)**

In the June 12, 2003 Office Action, the Examiner stated that claims 3, 9, 15-17, and 25 are rejected under 35 U.S.C. §112,

Applicants: Richard Deckelbaum et al.  
U.S. Serial No.: 10/033,629  
Filed: December 28, 2001  
Page 9

second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. The Examiner stated that claims 3, 9, 15 and their dependents, drawn to an emulsion, are rendered vague and indefinite for reciting "preferentially effects" because it is unclear if the limitations following the phrase are intended to be merely exemplary of the remainder of the claim, and therefore not required, or if the limitations are a required feature of the claims. The Examiner stated that the claims are further indefinite because it is unclear what effects are occurring. The Examiner stated that, for example, is the triglyceride increasing or decreasing delivery of the pharmaceutical agent. The Examiner stated that claim 25 is rendered indefinite because it depends on a non-elected claim. The Examiner further stated that applicants may prefer to change the dependency of claim 25 to claim 24.

In response, applicants respectfully traverse the Examiner's rejection. However, in order to expedite prosecution, and without conceding the correctness of the Examiner's position, applicants have amended claims 3, 9, 15, 24, and 25 to more distinctly claim the subject matter. Applicants further note that, in response to the Examiner's statement that that "the claims are further indefinite because it is unclear what effects are occurring", the claims as amended make it clear that the verb recited in claims 3, 9 and 15 is "effects" and not "affects". Accordingly, applicants maintain that the claims comply with the provisions of 35 U.S.C. §112, and request that the Examiner reconsider and withdraw this ground of rejection.

Applicants: Richard Deckelbaum et al.  
U.S. Serial No.: 10/033,629  
Filed: December 28, 2001  
Page 10

**Claims Rejected Under 35 U.S.C. §102**

The Examiner stated that claims 1-9, 11, and 24-25 are rejected under 35 U.S.C. §102(b) as being anticipated by Treskova et al. (September 1999). The Examiner stated that applicants claim an emulsion comprising a pharmaceutical agent, fish oil, and emulsifier. The Examiner stated that the fish oil is an omega-3-triglyceride and the composition is delivered to extrahepatic tissue, and the omega-3-triglyceride effects delivery of the pharmaceutical agent. The Examiner also stated that applicants additionally claim an emulsion comprising a pharmaceutical agent, a medium chain triglyceride, a long chain triglyceride, and an emulsifier, wherein the ratio of medium to long chain triglycerides is about 1 to 1, by weight. The Examiner stated that applicants claim an emulsion comprising a pharmaceutical agent, a fish oil, a medium chain triglyceride, a long chain triglyceride, and an emulsifier wherein the ration of medium chain to long chain triglycerides to fish oil is about 5 to 4 to 1 by weight. The Examiner also stated that the fish oil is an omega-3-triglyceride and the composition is delivered to an extrahepatic tissue and the omega-3-triglyceride effects delivery of the pharmaceutical agent to the tissue. The Examiner further stated that the compositions have 80% of the particles with a diameter of 150-350nm. The Examiner stated that, finally, applicants claim an emulsion comprising a pharmaceutical agent, triglyceride and emulsifier, wherein the triglyceride is a medium or long chain triglyceride.

The Examiner stated that Treskova et al. teaches therapeutic (pharmaceutical, thus containing a pharmaceutical agent) emulsions comprising emulsifiers, long chain triglycerides (LCT), medium chain triglycerides (MCT), and omega-3-fatty acids (triglycerides) in the form of fish oil, with emulsion

Applicants: Richard Deckelbaum et al.  
U.S. Serial No.: 10/033,629  
Filed: December 28, 2001  
Page 11

particle sizes of about 300nm (p.254). The Examiner also stated that the emulsions have a 1:1 ration of medium to long chain triglycerides, and a 5:4:1 ration of LCT:MCT: omega-3-triglycerides (fish oil) (Abstract, p.254). The Examiner further stated that Treskova et al. teaches the composition is such that omega-3-triglyceride increases delivery of the agent to extrahepatic tissues (abstract). The Examiner stated that the reference anticipates the claimed subject matter.

In response, applicants respectfully traverse the Examiner's rejection. Applicants note that Treskova et al. does not teach all the elements of the claimed invention. Specifically, Treskova et al. teaches using triglycerides themselves for clinical applications (for example, see Abstract, first sentence), but nowhere does Treskova et al. teach using compositions comprising triglycerides with a therapeutically effective amount of a pharmaceutical agent as claimed by applicants. Accordingly, Treskova et al. does not anticipate the claimed subject matter. Applicants thus maintain that the rejected claims comply with the provisions of 35 U.S.C. §102, and request that the Examiner reconsider and withdraw this ground of rejection.

The Examiner stated that claims 1-2, 4-6, 8, and 24-25 are rejected under 35 U.S.C. §102(b) as being anticipated by Pscherer et al. (U.S. Patent No. 6,008,248). The Examiner stated that applicants claim an emulsion comprising a pharmaceutical agent, fish oil and emulsifier, wherein the fish oil is an omega-3-triglyceride. The Examiner stated that applicants claim an emulsion comprising a pharmaceutical agent, a medium chain triglyceride, a long chain triglyceride and an emulsifier, wherein the medium chain to long chain triglycerides are in a ration of about 1 to 1, by weight. The Examiner stated that the applicants claim an emulsion

Applicants: Richard Deckelbaum et al.  
U.S. Serial No.: 10/033,629  
Filed: December 28, 2001  
Page 12

comprising a pharmaceutical agent, a fish oil, a medium chain triglyceride, a long chain triglyceride, and an emulsifier wherein the fish oil is an omega 3 triglyceride. The Examiner stated that applicants claim an emulsion comprising a pharmaceutical agent, triglyceride and emulsifier wherein the triglyceride is a medium or long chain triglyceride.

The Examiner stated that Pscherer et al. teaches lipid emulsions comprising MCT, LCT, omega-3-triglycerides in the form of fish oil, emulsifiers and vitamin E (a pharmaceutical agent) (col. 2-4). The Examiner stated that specifically, the composition contains 30-60% MCT, 40-85% LCT (combined vegetable and fish oils) col. 2, line 62 - col. 3, line 7), and 0.6-1.5% emulsifiers (col. 4, lines 20-25), and has particles sizes of less than 0.5 micrometers (col. 5, line 6-7). The Examiner stated that although Pscherer et al. does not teach the component amounts are predetermined to deliver pharmaceutical agents to predetermined tissues, the compositions appear to be the same. The Examiner stated that therefore the reference anticipates the claimed subject matter.

In response, applicants respectfully traverse the Examiner's rejection. However, in order to expedite prosecution, and without conceding the correctness of the Examiner's position, applicants have amended claims 1, 2, and 24 to more distinctly claim the subject matter. Applicants note that, as the Examiner states, Pscherer et al. discloses lipid emulsions comprising MCT and LCT and omega-3-triglycerides in the form of fish oil, and emulsifiers and vitamin E, in contrast to the subject matter recited in claims 1 and 2 which recite a composition in the form of an emulsion consisting of a therapeutically effective amount of a pharmaceutical agent, an amount of a fish oil predetermined so as to deliver the

Applicants: Richard Deckelbaum et al.  
U.S. Serial No.: 10/033,629  
Filed: December 28, 2001  
Page 13

pharmaceutical agent to a predefined tissue in a subject, and an amount of an emulsifier sufficient to result in the composition forming the emulsion. Additionally, the emulsion disclosed by Pscherer et al. comprises LCT, MCT, and fish oil, in contrast to claim 24. Accordingly, applicants maintain that the claims 1 and 2 comply with the provisions of 35 U.S.C. §102, and request that the Examiner reconsider and withdraw this ground of rejection.

The Examiner stated that claims 1-2, 10-11 and 24-25 are rejected under 35 U.S.C. §102(b) as being anticipated by Wretlind et al. (U.S. Patent No. 4,970,209). The Examiner stated that applicants claim an emulsion comprising a pharmaceutical agent, fish oil and emulsifier, wherein the fish oil is an omega-3-triglyceride. The Examiner stated that the composition has 80% of the particles with a diameter of 30-150 or 150-350nm. The Examiner stated that applicants additionally claim an emulsion comprising a pharmaceutical agent, triglyceride and emulsifier wherein the triglyceride is a medium or long chain triglyceride.

The Examiner stated that Wretlind et al. teaches emulsion compositions for delivering therapeutics (Abstract), the composition comprising fish oil, emulsifiers, pharmaceutical agents and LCT with particle sizes of 0.005-0.5 microns (5-500nm) (col. 4). The Examiner stated that since fish oil intrinsically contains omega-3-triglycerides, the reference anticipates the claimed subject matter.

In response, applicants respectfully traverse the Examiner's rejection. However, in order to expedite prosecution, and without conceding the correctness of the Examiner's position, applicants have amended claims 1, 2, and 24 to more distinctly claim the subject matter. Applicants note that the emulsions

Applicants: Richard Deckelbaum et al.  
U.S. Serial No.: 10/033,629  
Filed: December 28, 2001  
Page 14

disclosed by Wretlind et al. for therapeutic purposes contain "one or more substances preventing or retarding aggregation or agglutination" (see Abstract, also see col. 4, lines 49-53). Accordingly, Wretlind et al. does not anticipate the claimed subject matter. Applicants thus maintain that the claims 1, 2, and 24 comply with the provisions of 35 U.S.C. §102, and request that the Examiner reconsider and withdraw this ground of rejection.

The Examiner stated that claims 1-2, 4, 6-8 and 24-25 are rejected under 35 U.S.C. §102(b) as being anticipated by Boll et al. (DE 390 03 057 A1). The Examiner stated that applicants claim an emulsion comprising a pharmaceutical agent, fish oil and emulsifier, wherein the fish oil is an omega-3-triglyceride. The Examiner stated that applicants claim an emulsion comprising a pharmaceutical agent, a medium chain triglyceride, a long chain triglyceride and an emulsifier. The Examiner stated that applicants claim an emulsion comprising a pharmaceutical agent, a fish oil, a medium chain triglyceride, a long chain triglyceride, and emulsifier wherein the fish oil is an omega-3-triglyceride.

The Examiner stated that Boll et al. teaches lipid emulsions containing omega-3-fatty acids as fish oil, an emulsifier, MCT and tocopherols (a pharmaceutical agent) for endotracheal treatment (Abstract). The Examiner stated that although Boll et al. does not teach the component amounts are predetermined to delivery pharmaceutical agents to predetermined tissues, the composition is disclosed for endotracheal treatment. The Examiner stated that also, the compositions appear to be the same. The Examiner stated that therefore the reference anticipates the claimed subject matter.

In response, applicants respectfully traverse the Examiner's

Applicants: Richard Deckelbaum et al.  
U.S. Serial No.: 10/033,629  
Filed: December 28, 2001  
Page 15

rejection. However, in order to expedite prosecution, and without conceding the correctness of the Examiner's position, applicants have amended claims 1, 2, and 24 to more distinctly claim the subject matter. Applicants note that, as the Examiner states, Boll et al. discloses teaches lipid emulsions containing omega-3-fatty acids as fish oil, an emulsifier, MCT and tocopherols (a pharmaceutical agent), in contrast to the subject matter recited in claims 1 and 2 which recite a composition in the form of an emulsion consisting of a therapeutically effective amount of a pharmaceutical agent, an amount of a fish oil predetermined so as to deliver the pharmaceutical agent to a predefined tissue in a subject, and an amount of an emulsifier sufficient to result in the composition forming the emulsion. Additionally, the emulsion disclosed by Boll et al. comprises MCT and fish oil, in contrast to claim 24. Accordingly, applicants maintain that the rejected claims comply with the provisions of 35 U.S.C. §102, and request that the Examiner reconsider and withdraw this ground of rejection.

The Examiner stated that claims 1-2 and 24-25 are rejected under 35 U.S.C. §102(b) as being anticipated by Hamazaki et al. (JP 62-129216). The Examiner stated applicants claim an emulsion comprising a pharmaceutical agent, fish oil and emulsifier, wherein the fish oil is an omega-3-triglycerides. The Examiner stated that applicants claim an emulsion comprising a pharmaceutical agent, triglyceride and emulsifier wherein the triglyceride is a medium or long chain triglyceride.

The Examiner further stated that Hamazaki et al. teaches emulsion compositions comprising EPA (LCT) in the form of fish oil and an emulsifier (Abstract). The Examiner stated that Hamazaki et al. anticipates the claimed subject matter.



Applicants: Richard Deckelbaum et al.  
U.S. Serial No.: 10/033,629  
Filed: December 28, 2001  
Page 16

In response, applicants respectfully traverse the Examiner's rejection. Applicants note that Hamakazi et al. does not teach all the elements of the claimed invention. Specifically, Hamakazi et al. suggests using emulsion compositions comprising EPA (LCT) in the form of fish oil and an emulsifier themselves for clinical applications (for example, see Abstract, last sentence), but nowhere does Hamakazi et al. teach using compositions comprising emulsifiers and fish oils or triglycerides with a therapeutically effective amount of a pharmaceutical agent as claimed by applicants. Accordingly, applicants maintain that the rejected claims comply with the provisions of 35 U.S.C. §102, and request that the Examiner reconsider and withdraw this ground of rejection

**Claims Rejected Under 35 U.S.C. §103**

The Examiner stated that claims 1-11 and 24-25 are rejected under 35 U.S.C. §103(a) as being unpatentable over Treskova et al. The Examiner stated that applicants claim an emulsion comprising a pharmaceutical agent, fish oil and emulsifier. The Examiner stated that the fish oil is an omega-3-triglyceride and the composition is delivered to extrahepatic tissue, and the omega-3-triglyceride effects delivery of the pharmaceutical agent. The Examiner stated that the applicants additionally claim an emulsion comprising a pharmaceutical agent, a medium chain triglyceride, a long chain triglyceride and an emulsifier wherein the ration of medium to long chain triglycerides is about 1 to 1, by weight. The Examiner stated that applicants claim an emulsion comprising a pharmaceutical agent, a fish oil, a medium chain triglyceride, a long chain triglyceride, and an emulsifier wherein the ration of medium chain to long chain triglycerides to fish oil is about 5 to 4 to 1 by weight. The Examiner stated that the fish oil is an

omega-3-triglyceride and the composition is delivered to an extrahepatic tissue and the omega-3-triglyceride effects delivery of the pharmaceutical agent to the tissue. The Examiner stated that the compositions have 80% of the particles with a diameter of 30-150 or 150-350nm. The Examiner stated that finally applicants claim an emulsion comprising a pharmaceutical agent, triglyceride and emulsifier wherein the triglyceride is a medium or long chain triglyceride.

The Examiner stated that Treskova et al. teaches therapeutic (pharmaceutical, thus contain a pharmaceutical agent) emulsions comprising emulsifiers, long chain triglycerides (LCT), medium chain triglycerides (MCT), and omega-3-fatty acids (triglycerides) in the form of fish oil, with emulsion particle sizes of about 300nm (p.254). The Examiner stated that the emulsions have a 1:1 ration of medium to long chain triglycerides, and a 5:4:1 ration of LCT:MCT: omega-3-triglycerides (fish oil) (Abstract, p.254). The Examiner stated that Treskova et al. teaches the composition is such that omega-3-triglyceride increases delivery of the agent to extrahepatic tissues (Abstract).

The Examiner further stated that although Treskova et al. does not teach the emulsions with particle sizes of 30-150nm, it would have been well within the purview of one of ordinary skill in the art to optimize particle size as a matter of routine experimentation (see other cited references for support). The Examiner stated that therefore, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by routine practice to optimize the emulsion particle size of Treskova et al. with a reasonable expectation for successfully obtaining an effective emulsion composition.

Applicants: Richard Deckelbaum et al.  
U.S. Serial No.: 10/033,629  
Filed: December 28, 2001  
Page 18

In response, applicants respectfully traverse the Examiner's rejection. Applicants note that Treskova et al. does not teach all the elements of the claimed invention. Specifically, Treskova et al. teaches using triglycerides themselves for clinical applications (for example, see Abstract, first sentence), but nowhere does Treskova et al. teach using compositions comprising triglycerides with a therapeutically effective amount of a pharmaceutical agent as claimed by applicants. Accordingly, Treskova et al. does not anticipate the claimed subject matter. Applicants thus maintain that the rejected claims comply with the provisions of 35 U.S.C. §103, and request that the Examiner reconsider and withdraw this ground of rejection.

The Examiner stated that claims 1-11, 15-17, and 24-25 are rejected under 35 U.S.C. §103(a) as being unpatentable over Treskova and Counsell et al. (U.S. patent No. 5,985,941). The Examiner stated that applicants claim an emulsion comprising a pharmaceutical agent, fish oil and emulsifier. The Examiner stated that the fish oil is an omega-3-triglyceride and the composition is delivered to extrahepatic tissue, and the omega-3-triglyceride effects delivery of the pharmaceutical agent. The Examiner stated that applicant additionally claims an emulsion comprising a pharmaceutical agent, a medium chain triglyceride, a long chain triglyceride and an emulsifier wherein the ratio of medium to long chain triglycerides is about 1 to 1, by weight. The Examiner stated that applicants claim an emulsion comprising a pharmaceutical agent, a fish oil, a medium chain triglyceride, a long chain triglyceride, and an emulsifier wherein the ration of medium chain to long chain triglycerides to fish oil is about 5 to 4 to 1 by weight. The Examiner stated that the fish oil is an omega-3-triglyceride and the composition is delivered to an extrahepatic tissue and the omega-3-triglyceride effects

delivery of the pharmaceutical agent to the tissue. The Examiner stated that the compositions have 80% of the particles with a diameter of 30-150 or 150-350nm. The Examiner stated that applicants claim an emulsion comprising a pharmaceutical agent to a tissue, and the ligand effects delivery of the agent. The Examiner stated that the ligand is apolipoprotein E, specifically human apolipoprotein E or homologs thereof differing by less than 3 amino acids and having activity of human apolipoprotein E. The Examiner stated that, finally, applicants claim an emulsion comprising a pharmaceutical agent, triglyceride and emulsifier wherein the triglyceride is a medium or long chain triglyceride.

The Examiner stated that Treskova et al. teaches therapeutic (pharmaceutical, thus contain a pharmaceutical agent) emulsions comprising emulsifiers, long chain triglycerides (LCT), medium chain triglycerides (MCT), and omega-3-fatty acids (triglycerides) in the form of fish oil, with emulsion particle sizes of about 300nm (p.254). The Examiner stated that the emulsions have a 1:1 ration of medium to long chain triglycerides, and a 5:4:1 ration of LCT:MCT: omega-3-triglycerides (fish oil) (Abstract, p.254). The Examiner stated that Treskova teaches the composition is such that omega-3-triglyceride increases delivery of the agent to extrahepatic tissues (Abstract).

The Examiner stated that Counsell et al. teaches emulsions for hepatic tissue selective delivery of pharmaceuticals (Abstract), comprising a lipophilic core and emulsifier (col. 5, line 50-59). The Examiner stated that the core may contain LCT and fish oils (col. 5, line 66 - col. 6, line 9, and col. 11), and the emulsion particle size is 50-200nm (Abstract).

The Examiner stated that the above references do not

specifically teach the emulsions comprising the ligand apolipoprotein E, or homologs thereof. The Examiner stated that however, Treskova et al. does suggest that uptake of the triglycerides are increased in the presence of apolipoprotein E (p.257). The Examiner stated that in addition, Counsell et al. teaches that the emulsion must associate with apolipoprotein E to make it hepatocyte specific (col. 4-5). The Examiner stated that at the time of the claimed invention, one of ordinary skill in the art would have been motivated by the teachings of Treskova et al. and Counsell et al. to include apolipoprotein E, or homologs thereof, in the disclosed compositions for it's specificity to hepatic and extrahepatic tissues, and for the disclosed effect of increasing triglyceride uptake. The Examiner stated that moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by Treskova et al. and Counsell et al. to include apolipoprotein E or homologs thereof in the compositions with a reasonable expectation for successfully obtaining an emulsion for delivering and agent to extrahepatic tissue.

In response, applicants respectfully traverse the Examiner's rejection. Applicants note that the cited references combined do not teach all the elements of the claimed invention. Specifically, Treskova et al. teaches using triglycerides themselves for clinical applications (for example, see Abstract, first sentence), but nowhere does Treskova et al. teach using compositions comprising triglycerides with a therapeutically effective amount of a pharmaceutical agent as claimed by applicants. Moreover, Counsell et al. does not cure this deficiency.

Additionally, applicants note that the cited references combined do not teach or suggest an emulsion composition

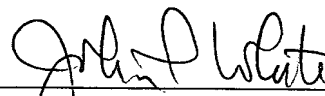
Applicants: Richard Deckelbaum et al.  
U.S. Serial No.: 10/033,629  
Filed: December 28, 2001  
Page 21

comprising apolipoprotein, as acknowledged by the Examiner in the June 12, 2003 Office Action, and the Examiner has failed to point to where the references teach or suggest an emulsion composition comprising apolipoprotein, rather than separate plasma lipoproteins that the emulsion can be exposed to (see Counsell et al., col 4, lines 39-42 and 47-48). Accordingly, applicants thus maintain that the rejected claims comply with the provisions of 35 U.S.C. §103, and request that the Examiner reconsider and withdraw this ground of rejection.

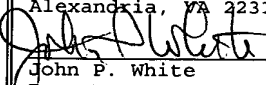
If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

No fee is deemed necessary in connection with the filing of this Amendment. If any fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450 Alexandria, VA 22313-1450	
 John P. White Reg. No. 28,678	9/12/03 Date